ALPHA DIAGNOSTIC INTERNATIONAL

LIFE TECH Life Technologies™ Your Molecular & Cell Technology Partner

Ebola & Marburg Virus Vaccine ELISA Kits, Recombinant Proteins, and Antibodies

Alpha Diagnostic Intl Inc. (ADI) has developed many prototype vaccines and ELISA tests to determine the efficacy of Ebola candidate vaccines in animals and humans. We have cloned and expressed several Ebola viral proteins (GP, NP, and VP40) from Ebola/Marburg viruses, generated antibodies, and developed ELISA kits for the detection and measurement of Ebola related antigens and antibodies. ADI's Ebola kits contain all animal derived antibodies made to purified recombinant proteins. ADI antibodies and kits have no Ebola virus or viral derived proteins and are completely safe to use and transport. The kits have been tested and validated with therapeutic antibodies, Zmapp. Additional ELISA kits and antibodies are available for Ebola vaccine vectors (Adenovirus, VSV, and Rabies virus proteins) to determine efficacy of Ebola vaccines.

Zaire-Ebola vaccine Related ELISA kits

(See Details at the website) http://4adi.com/commerce/catalog/spcategory.jsp?category_id=2762

Vaccines	Target Antigens	ELISA Type	Ab Type	Human	Mouse	Monkey	Rabbit	Others
Ebola	Zaire-NP	Ab	IgG	AE-320620-1	AE-320600-1	AE-320650-1	AE-320640-1	
			IgM	AE-320630-1	AE-320610-1	AE-320660-1		
	Zaire-GP	Ab	IgG	AE-320620-1	AE-320600-1	AE-320650-1	AE-320640-1	
			IgM	AE-320630-1	AE-320610-1	AE-320660-1		
	Zaire-VP40	Ab	IgG	AE-320720-1	AE-320700-1	AE-320750-1	AE-320740-1	
			IgM	AE-320730-1	AE-320710-1	AE-320760-1		
	Humanized	Ab	#AE-320810; Humanized (plant expressed) Anti-Ebola GP IgGs ELISA kit					
			#AE-320800-48; Zaire Ebola Virus Glycoprotein (EBOV GP antigen) ELISA Kit					
			#AE-320815; Anti-Humanized Ebola GP IgGs (Anti-drug antibody/ADA) ELISA kit					
	Sudan-NP	Ab	IgG	AE-321620-1	AE-321600-1	AE-321650-1	AE-321640-1	
			IgM	AE-321630-1	AE-321610-1	AE-321660-1		
	Sudan-GP	Ab	IgG	AE-321620-1	AE-321600-1	AE-321650-1	AE-321640-1	
			IgM	AE-321630-1	AE-321610-1	AE-321660-1		
	Reston-Gp	Ab	IgG	AE-321620-1		AE-321630-1		Sw, Gp
	Combo-GP	Ab	IgG	AE-325600-XH		AE-325600-XM	Zaire+Sudan+Reston+Bundibugyo	
Ebola/Marburg	Marburg-GP	Ab	IgG	AE-321620-1	AE-321600-1	AE-321650-1		
			IgM	AE-321630-1	AE-321610-1	AE-321660-1		
	Angola-GP	Ab	IgG	AE-322620-1	AE-322600-1	AE-322650-1		
			IgM	AE-322630-1	AE-322610-1	AE-322660-1	AE-322640-1	
	Tai Forest-GP	Ab	IgG	AE-325620-1				

Note: additional ELISA kits for pig, G. pig, dog and other species also available. Please contact ADI. All of the above ELISA kits are for research use only (RUO) and not for diagnostic, therapeutic or prevention of the disease.

Ebola Vaccine/Vector ELISA kits

There is a critical and immediate need for new **Ebola vaccines**. WHO has recommended two candidate vaccines for clinical testing. One (**cAd3-ZEBOV**) has been developed by GlaxoSmithKline (GSK) in collaboration with the US National Institute of Allergy and Infectious Diseases (NIAID). It uses a chimpanzee-derived adenovirus vector with an Ebola virus gene inserted. The second (**rVSV-ZEBOV**) was developed by the Public Health Agency of Canada in Winnipeg. The license for commercialization of the Canadian vaccine is held by an American company, the NewLink Genetics Company, located in Ames, Iowa. The vaccine uses an attenuated or weakened vesicular stomatitis virus Indiana (VSVI), a pathogen found in livestock; one of its genes has been replaced by an Ebola virus gene. The trials, which are being conducted in healthy human volunteers, are designed to test safety and immunogenicity and select the appropriate dose. Positive results have been reported from both vaccines (refs 1).
References: (1) http://www.nature.com/news/us-ebola-vaccine-trial-reports-positive-results-1.16417;

Type	Product Description	Ab Type	Mouse	Human	Monkey/Chimp
New AD5 Vaccines	Adenovirus hexon antibody ELISA Kits**	IgG	AE-327100-1	AE-327110-1	AE-327120-1
rVSV vaccines	VSV Indiana Matrix (M) antibody ELISA Kits**	IgG	AE-327200-1	AE-327210-1	AE-327220-1
	VSV Indiana Glycoprotein antibody ELISA Kits**	IgG	AE-327300-1	AE-327310-1	AE-327320-1

Rabies or vaccinia virus vector ELISA kits are also available.
http://4adi.com/commerce/ccc2726-rabies-vaccine-elisa-and-reagents-**rabies**-vaccine--elisa-reagents.htm
http://4adi.com/commerce/ccc2745-vaccinia-virus-based-vaccines-and-elisa-kits-**vaccinia**-virus--vaccines--elisa-kits0d0a.htm

Zaire-Ebola Vaccine Related Antibodies, Proteins and other Reagents

Virus Type	Protein	Catalog#	Product Description	Product Type
Bundibugyo	GP1/2 RBD	BVGP45-R-10	Recomb. (sf9) Bundibugyo **GP** (Uganda 2007,1-501aa, his tag, >95%)	Rec. protein
		BVRB46-R-10	Recomb. (HEK) Bundibugyo GP **RBD domain** (hIgG1-Fc-tag at CT)	Rec. protein
		BVRB46-BTN	Biotin-Recomb. (HEK) Bundibugyo GP **RBD domain** (hIgG1-Fc-tag at CT)	Rec. protein
Zaire Ebola	**Glycoprotein** GP1/2	EVGP15-A	Rabbit Anti-Zaire Ebola virus **glycoprotein** (1-676aa/DNA vaccine) IgG	Antibodies
		EVGP16-A	Rabbit Anti-Zaire Ebola virus **glycoprotein** (1-652aa/DNA vaccine) IgG	Antibodies
		EVGP20-R-10	Recomb. (sf9) Zaire EVGP (GIN/2014/Makona-C15, 1-650aa, his-tag at CT)	Rec. protein
		EVGP21-R-10	Recomb. (HEK) Zaire EVGP (GIN/2014/1-650aa, his-tag at CT, >95%), Low endotoxin	Antigen protein
		EVGP22-A	Goat Anti-Zaire Ebola virus (Mayinga) glycoprotein (ZEBOV GP) IgG,	Antibodies
		EVGP31-R-10	Recomb. (HEK) Zaire EV**GP** (Mayinga, 1-650aa, his-tag at CT, >95%)	Rec. protein
		EVGP31-BTN	Biotin-Recomb. (HEK) Zaire **EVGP** (Mayinga, 1-650aa, his-tag at CT)	Rec. protein
	GP1	EVGP33-R-10	Recomb. (HEK) Zaire EVGP1 (GIN/2014/ GP1, 1-501aa, his-tag, >95%)	Rec. protein
		EVGP18-R-10	Recomb. (sf9) Zaire EVGP**1** (GIN/2014/ Makona 1-501aa, his-ta at CT)	Rec. protein
	GP2	EVGP32-R-10	Rec. (HEK) Zaire EVGP2 (GIN/2014/ Makona, **GP2**, 501-650aa, mFc-tag)	Rec. protein
	GP/RBD	EVRB11-R-10	Recomb. (HEK) **Zaire** EVGP **RBD domain** (1-308aa, GIN/2014/, **his-tag at CT)**	Rec. protein
		EVRB11-BTN	Biotin- Rec. (HEK) **Zaire** EVGP-**RBD domain** (1-308aa, GIN/2014/**his-tag at CT)**	Rec. protein
		EVRB14-R-10	Recomb. (HEK) Zaire EVGP **RBD** domain (Mayinga 1-308 aa, his tag)	Rec. protein
		EVRB14-BTN	Biotin- Recomb. (HEK) Zaire EVGP-**RBD** domain (Mayinga, 1-308 aa, his tag, >95%)	Rec. protein
		EVNP11-S	Rabbit Anti-Zaire-Ebola virus **NP** (Mayinga EBOV NP) protein antiserum	Antiserum
		EVNP13-A	Rabbit Anti-Zaire Ebola virus **NP** (EBOV NP, 1-739/DNA vaccine) IgG	Antibodies
		EVNP15-R-10	Recomb. (E.coli) Zaire Ebola **NP** (full length, his-tag, 82 kda), purified	Rec. protein
		EVNP16-R-10	Recomb. (E.coli) EBOV NP) (GIN/2014/Kissidougou-C15, 630-739aa, his-tag, >95%)	Rec. protein
	VP24	EVP24-R-10	Recomb. (E.coli) Zaire Ebola virus **VP24** (1-233aa, his tag, >95%)	Rec. protein
	VP40	EVP404-A	Goat Anti-Zaire-Ebola virus (Mayinga) VP40 (ZEBOV VP40) IgG, purified	Antibodies
		EVP406-R-10	Recomb. (E.coli) Zaire Ebola virus **VP40** (GIN/2014/ 1-326 aa, his-MBP tag, >95%)	Rec. protein
		EVP406-BTN	Biotin-Recomb. (E.coli) Zaire Ebola virus **VP40** (GIN/2014/ 1-326 aa, his-MBP tag, >95%)	Rec. protein
	Virus	EVZ12-M	Mouse Monoclonal Anti-Zaire Ebola virus (killed) IgG, aff pure	Antibodies
		EVZ13-M	Mouse Monoclonal Anti-Zaire Ebola virus (Killed) IgG, aff pure	Antibodies
		EVZ14-M	Mouse Mono Anti-Zaire Ebola virus IgG (mixture of EVZ12-M and EVZ13-M)	Antibodies
	Peptides	SP-89925-1	Zaire Ebola virus Glycoprotein (GP), T cell epitope (577-584) (MW: 966.1)	Pure peptide
		SP-89926-1	Zaire Ebola virus negative control peptide for SP-89925-1 (MW: 1102.2)	Pure peptide
Sudan Ebola	Glycoprotein/GP	SVGP24-R-10	Recom. (HEK) Sudan-Ebola virus **GP** (Gulu, 1-637aa, his-tag at CT, >95%	Rec. protein
		SVGP24-BTN	Biotin-Recom. (HEK) Sudan-Ebola virus **GP** (Gulu, 1-637aa, >95%, his-tag	Rec. protein
		SVGP29-R-10	Rec. (HEK) Sudan-Ebola virus **GP** (Uganda, 1-637aa, his-tag at CT, >95	Rec. protein
	GP1 /RBD Domain	SVGP28-R-10	Rec. (HEK) Sudan Ebola virus **GP 1** (Uganda, 1-501aa, his-tag, >95%)	Rec. protein
		SVRB11-R-10	Rec. (**HEK**) Sudan-EVGP **RBD domain** (Uganda-00/1-320aa, his-tag)	Rec. protein
	NP	SVNP27-R-10	Recomb. (E.coli) Sudan **EBOV NP** (Uganda, 630-738aa, his-tag, >95%)	Rec. protein
	VP40	SVP407-R-10	Recomb. (E. coli) Sudan **VP40** (Uganda,1-326aa, his tag, >95%)	Rec. protein
		SVP408-R-10	**Rec.** (E. coli) Sudan **VP40** (Uganda,1-326aa, his-MBP tag at NT, >95%)	Rec. protein
Reston	RVGP	RVGP31-A	Rabbit anti-Reston GP) peptide IgG aff pure	Antibodies
		RVGP35-R-10	Recomb. (sf9) **REBOV GP** minus transmembrane domain, his-tag, 72 kda), purified	Rec. protein
		RVGP35-R-100	Recomb. (sf9) **REBOV GP** minus transmembrane domain, his-tag, 72 kda), purified	Rec. protein
New Tai Forest	TAFV GP	TVGP55-R-10	Rec. (E. coli) Tai Forest Ebola virus glycoprotein (**TAFV GP** his-tag), purified	Rec. protein
		TVGP51-S	Rabbit anti-TAFV GP antiserum	Antibodies
Marburg	MARV-GP	MVGP12-A	Rabbit Anti-Marburg virus glycoprotein peptide (MARV GP) IgG, aff pure	Antibodies
		MVGP13-M	Mouse Monoclonal Anti-Marburg virus glycoprotein (MARV GP) IgG, purified	Antibodies
		MVGP15-R-10	Recomb. (sf9) Marburg virus glycoprotein (Angola, his-tag, >95%), purified	Antibodies
		MVGP16-BTN	Biotin-Recomb. (sf9) Marburg virus glycoprotein (Musoke, HA-tag, >95%), purified	Antibodies
		MVGP16-R-10	Recomb. (sf9) Marburg virus glycoprotein (Musoke, HA-tag, >95%), purified	Antibodies
		MVGP17-A	Rabbit Anti-MARV GP 26-649 aa/Muskoe/DNA vaccine) IgG, aff pure	Antibodies
		MVGP18-A	Rabbit Anti-MARV GP 26-649 aa/Popp/DNA vaccine) IgG, aff pure	Antibodies

Adenovirus, Rabies and VSV are being used to express Ebola genes (vaccines). ADI has many antibodies, recombinant proteins and ELISA kits for these vectors.

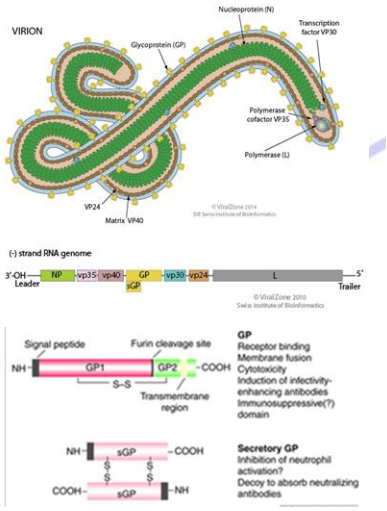
Ebola_Marburg_Vaccines_ELISA_Flr 160605A

Ebola Virus –General Information, Therapeutics and Vaccines

Ebola virus (**EBOV**) causes severe disease in humans and in nonhuman primates in the form of viral hemorrhagic fever. The name Ebola virus is derived from the Ebola River (a river that was at first thought to be in close proximity to the area in Zaire where the first recorded Ebola virus disease outbreak occurred) and the taxonomic suffix virus. Zaire Ebolavirus is a virological taxon included in the genus Ebolavirus, family Filoviridae, and order Mononegavirales. The family Filoviridae (members are called Filovirus or filovirids; filum is derived from latin meaning filamentous) is a group of several related viruses that form filamentous infectious viral particles (virions) and encode their genome in the form of single-stranded negative-sense RNA. The family currently includes the three virus genera Cuevavirus, Ebolavirus, and Marburg virus. The family members are:

Genus name	*Species name*	*Virus name (Abbreviation)*
Cuevavirus	*Lloviu cuevavirus**	Lloviu virus (LLOV)
Ebolavirus	*Bundibugyo ebolavirus*	Bundibugyo virus (BDBV; previously BEBOV)
	Reston ebolavirus	Reston virus (RESTV; previously REBOV)
	Sudan ebolavirus	Sudan virus (SUDV; previously SEBOV)
	Taï Forest ebolavirus	Taï Forest virus (TAFV; previously CIEBOV)
	*Zaire ebolavirus**	Ebola virus (EBOV; previously ZEBOV)
Marburgvirus	*Marburg marburgvirus**	Marburg virus (MARV)

The two members of the family that are commonly known are Ebola virus and Marburg virus. Both viruses, and some of their lesser known relatives, cause severe disease in humans and nonhuman primates (NHP) in the form of viral hemorrhagic fevers. All Ebola viruses and Marburg viruses are Select Agents Group 4 Pathogens. Filoviruses have a history that dates back several tens of millions of years. The most recent common ancestor of both the Reston and Zaire species has been estimated to be ~1960. The most recent common ancestor of the Marburg and Sudan species appears to have evolved 700 and 850 years before present respectively. The family Filoviridae represents significant health risks as emerging infectious diseases as well as potentially engineered biothreats. Ebolavirus species Zaire (ZEBOV) causes a highly lethal hemorrhagic fever, resulting in the death of 90% of patients within days. Ebola Zaire attacks every organ and tissue in the human body except skeletal muscle and bone. Ebola is classified as a Level 4 pathogen (higher than AIDS) with a 2 to 21 day (7 to 14 days average) incubation period. There are currently four known strains of Ebola: Zaire, Sudan, Reston and Tai. All of them cause illness in sub-human primates. Only Ebola Reston does not cause illness in humans. The mortality rate of Ebola victims is between 60% and 90%; with Ebola Sudan at 60% and Ebola Zaire at 90%.



The virions are tubular in general form but variable in overall shape and may appear as the classic shepherd's crook or eyebolt, as a U or a 6, or coiled, circular, or branched. Ebolavirions consist of seven structural proteins. At the center is the helical ribonucleocapsid, which consists of the genomic RNA wrapped around a polymer of **nucleoproteins (NP).** Associated with the ribonucleoprotein is the RNA-dependent RNA polymerase (L) with the polymerase cofactor (VP35) and a transcription activator (VP30). The ribonucleoprotein is embedded in a matrix, formed by the major (**VP40**) and minor (VP24) matrix proteins. These particles are surrounded by a lipid membrane derived from the host cell membrane. The membrane anchors **a glycoprotein (GP1,2**) that projects 7 to 10 nm spikes away from its surface. While nearly identical to marburgvirions in structure, ebolavirions are antigenically distinct. Being acellular, viruses do not grow through cell division; instead, they use the machinery and metabolism of a host cell to produce multiple copies of themselves, then assembling in the cell.

Ebola virus disease (EVD) is clinically indistinguishable from **Marburg virus disease (MVD)** and can be easily be confused with many other diseases prevalent in Equatorial Africa, such as other viral hemorrhagic fevers, falciparum malaria, typhoid fever, shigellosis, and rickettsial diseases such as typhus, cholera, gram-negative septicemia, borreliosis such as relapsing fever or EHEC enteritis. The most common **diagnostic methods** are therefore RT-PCR in conjunction with antigen-capture ELISA which can be performed in field or mobile hospitals and laboratories. **Vaccines** have successfully protected nonhuman *primates*; however, the six months needed to complete immunization made it impractical in an epidemic. In 2003, a vaccine using an adenoviral (ADV) vector carrying the Ebola spike protein was tested on crab-eating macaques. The monkeys were challenged with the virus 28 days later, and remained resistant. In 2005, a vaccine based on attenuated recombinant vesicular stomatitis virus (VSV) vector carrying either the Ebola glycoprotein or Marburg glycoprotein successfully protected nonhuman primates, opening clinical trials in humans. There are currently **no Food and Drug Administration-approved vaccines** for the prevention of EVD. The most promising ones are DNA vaccines or are based on adenoviruses, vesicular stomatitis Indiana virus (VSIV) or filovirus-like particles (VLPs) as all of these candidates could protect nonhuman primates from Ebola virus-induced disease.

Experimental Drugs and Vaccines (ZMapp, Favipravir, TKM-Ebola etc)

From 1976 (when it was first identified) through 2013, the WHO reported a total of 1,716 cases. The largest outbreak to date is the ongoing 2014 West Africa Ebola outbreak, which is affecting Guinea, Sierra Leone, Liberia and Nigeria. As of 26 August 2014, 3,069 suspected cases resulting in the deaths of 1,552 have been reported. Currently, neither a specific treatment nor a vaccine licensed for use in humans is available. However, a number of vaccine candidates have been developed in the last decades that are highly protective in non-human primates. Among these vaccines are recombinant Adenoviruses (Ad5/chAd3), recombinant Vesicular Stomatitis viruses (VSV), recombinant Human Parainfluenza viruses and virus-like particles. There is sufficient evidence from studies in animal studies and NHP (non-human primates) that a vaccine protective against ebolaviruses is possible.

Ebola Therapeutics

The FDA has allowed two drugs, **ZMapp** and an RNA interference drug called **TKM-Ebola**, to be used in people infected with Ebola under these programs during the 2014 outbreak. **ZMapp**, the top-secret magic serum, is an experimental biopharmaceutical drug comprising three humanized monoclonal antibodies (anti-Zaire Ebola GP) under development as a treatment for Ebola virus disease. The ZMapp drug is being developed by Mapp Biopharmaceutical Inc., a result of the collaboration between Mapp Biopharmaceutical (San Diego), LeafBio (the commercial arm of Mapp Biopharmaceutical), Defyrus Inc. (Toronto), the U.S. government and the Public Health Agency of Canada. ZMapp is composed of three monoclonal antibodies (mAbs) that have been humanized by genetic engineering and combine "the best components of MB-003 (Mapp) and ZMAb (Defyrus/PHAC)", each of which were combinations of mAbs. Zmapp components are humanized monoclonal antibody c13C6 from MB-003 and two

humanized mAbs from ZMab, c2G4 and c4G7. Like intravenous immunoglobulin therapy, ZMapp contains neutralizing antibodies that provide passive immunity to the virus by directly and specifically reacting with virus GP in a "lock and key" fashion. ZMapp is manufactured in the tobacco plant Nicotiana benthamiana in the bioproduction process known as "pharming" by Kentucky BioProcessing, a subsidiary of Reynolds American. **ADI has developed the first rapid ELISA kit to measure the activity or potency of the drug during its manufacturing. The kit also allows the measurement of active drug in serum or plasma of animals or humans**.

TKM-Ebola is being developed by Tekmira Pharmaceuticals Corp., a company located in Vancouver, Canada. The drug was formerly known as Ebola-SNALP. It is a combination of Small interfering RNAs (siRNAs) targeting three of the seven proteins in Ebola virus: Zaire Ebola L polymerase, Zaire Ebola membrane-associated protein (VP24), and Zaire Ebola polymerase complex protein (VP35), formulated with Tekmira's lipid nanoparticle technology. ADI has produced recombinant proteins, antibodies, and antibody ELISA kits to research the efficacy of TKM-Ebola therapy.

Current and Future Ebola Vaccines

A number of vaccines have been successfully tested in animals and NHP. Human safety studies of an experimental **Ebola vaccine developed by the National Institutes of Health (NIH) and GlaxoSmithKline will launch in September 2014**. NIH is also working with Crucell, Profectus Biosciences, Immunovaccine and researchers at Thomas Jefferson University to develop other candidate vaccines for Ebola. Human trials of the Crucell vaccine are planned for late 2015 or early 2016. Another experimental **Ebola vaccine, VSV-EBOV**, has been developed by the Public Health Agency of Canada and is licensed to NewLink Genetics. The clinical trials are expected to begin soon. NIAID also is funding Profectus Biosciences, a Baltimore, Maryland-based biotechnology company, to develop a candidate vaccine targeting **Ebola and Marburg infections**. The vaccines is based upon recombinant vesicular stomatitis Indiana virus (rVSV) vectored vaccines for EBOV and MARV glycoproteins (rVSV vector-GP construct (delta G1,2). This highly attenuated genetically modified rVSV vector is a replicating virus with good immunogenicity and low virulence. This strategy may mitigate the risk of poor of immunogenicity in vaccine recipients with immunologic memory to vector variants delivered in previous vaccinations. This vaccine is currently in preclinical testing.

Human trials of the candidate Ebola vaccine, co-developed by the US National Institutes of Health (NIH) and GlaxoSmithKline (GSK), are scheduled to start in September 2014 in the UK, The Gambia and Mali. The candidate vaccine is against the Zaire species of Ebola, which is the one circulating in West Africa, and uses a single **Zaire Ebola virus glycoprotein protein (GP)** to generate an immune response. NIAID is testing this same vaccine in the USA (**VRC 207 study**) in addition to a related vaccine that is designed to protect against two Ebola species (**Ebola Zaire and Ebola Sudan**). The NIAID/GSK Ebola vaccine candidate is based on an attenuated strain of chimpanzee cold virus, called chimp adenovirus type 3 (**ChAd3**). This approach uses ChAd vectors to obviate the issue of background immunity to human Ad5 vectors. The adenovirus is used as a carrier, or vector, to deliver benign genetic material derived from the Ebola virus Zaire species that has caused the current Ebola outbreak in West Africa. The genetic material contained in the investigational vaccine cannot cause a vaccinated individual to become infected with Ebola. The vaccine candidate delivers the Ebola genetic material to human cells but does not replicate further. Rather, the Ebola gene that it carries allows the cells of the vaccine recipient to express a single Ebola protein, and that protein prompts an immune response in the individual. The vaccine has shown promising protection in non-human primates (NHP) exposed to Ebola without significant adverse effects.

NIAID support is assisting Crucell (a Netherlands based biotechnology company) and Bavarian Nordic, based in Denmark. Crucell is developing a **multivalent Ebola/Marburg vaccine** using a recombinant adenovirus platform. Phase 1 clinical trial of this candidate vaccine is anticipated to begin by late 2015. The Multivalent **filovirus vaccine is based on recombinant adenovirus (Ad) vectors Ad26 and Ad35** that infect humans at low seroprevalence. Protective efficacy studies to date have all involved an Ad26 prime and an Ad35 boost with various viral GP antigens (EBOV, SUDV, MARV, and TAFV), followed by an exposure of four weeks after the boost immunization.

NIAID and Thomas Jefferson University in Philadelphia have developed an investigational **Ebola vaccine using the established rabies virus vaccine** platform. Ebola virus (EBOV) vaccine platform is based on: (a) replication competent rabies virus (RABV); (b) replication-deficient RABV;or (c) chemically inactivated RABV expressing EBOV glycoprotein (GP). The vaccines were found to be safe and produced potent immune responses against both rabies and Ebola viruses when tested in nonhuman primates. NIAID supported researchers are currently pursuing the development of multivalent vaccine candidates against Ebola, Marburg and rabies viruses for use in humans.

DoD-USAMRIID is working on a **VLP (virus like particles) vaccine for filoviruses**. VLPs are virus-sized particles formed by viral proteins (EBOV and MARV glycoproteins) which retain virus morphology but are noninfectious. VLPs have the advantages of rapid production in large quantities and generate robust innate, humoral and cellular immunity in rodents, NHPs and humans. There are no issues regarding vector immunity. A single vaccine may be effective against EBOV, SUDV, and MARV.

University of Texas at Austin researchers are evaluating the mucosal vaccine against **EBOV GP using an Ad5-based vaccine**. The goal is a vaccine that provides systemic and mucosal immunity with memory, low toxicity, and ease of administration and delivery.

Researchers at the University of Hawaii are exploring **recombinant filovirus antigens (GP1.2, VP24, and VP40) as vaccines**. Advantages of the subunit approach include the ability to precisely select antigen doses and the elimination of translation of protein antigens in the host.

Summary of Human and Animal Testing for Ebola Virus Antibodies

Some non-vaccinated and presumably non-Ebola virus exposed human samples showed the presence of VP40 and GP IgG and IgM but not the NP antibodies. Out of the 3 Ebola virus antibodies, anti-VP40 IgG and IgM appear to be present at higher concentrations and therefore may appear to be more prevalent than GP and NP. Interestingly, other potential mammals (Monkey/primates and pig) have no detectable level or very low levels. Our preliminary but limited data in humans clearly suggests that there is a significant immunity to Ebola virus in non-vaccinated populations, even in areas that are outside the Ebola epidemic, i.e., USA. Clearly, more work needs to be done to determine the source of Ebola virus antibodies and its significance.

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